REMARKS

Status of the Claims

Claims 1-20, 36, and 37 are pending. Claim 37 is amended to correct antecedent basis. No new matter is added.

Rejections Under 35 U.S.C. § 1112, 2nd Paragraph

Claim 37 stands rejected as lacking insufficient antecedent basis because claim 36 is drawn to a product, not a method.

Claim 37 is amended to recite "The resorbable implant material of claim 36." Accordingly, this rejection is moot.

Rejections Under 35 U.S.C. § 103

Claims 1-5, 8, 10-16, 18-20, 36, and 37 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Glajch in view of Brow and Yashchishin, and in further view of Day et al. (U.S. Patent No. 5,011,797, hereinafter "Day").

The USPTO contends that Glajch discloses a glass particle/implant that comprises radionuclides and has nitrogen incorporated in the glass, but does not disclose a nitrogen layer on the surface of the particle/implant.[1] To remedy this missing teaching, the USPTO cites Brow and Yashchishin, and asserts that it would have been obvious to "substitute" the nitrogen layer of Brow and/or Yashchishin "for the nitration of Glajch as the simple substitution of one known, equivalent element for another yields predictable results…"[2]

Applicant respectfully traverses.

A. The nitriding methods of Glajch and Brow and/or Yashchishin are not equivalents.

1. The dissolution rates of Glach's glass and Brow's and/or Yashchishin's glasses are significantly different.

Glajch suggests incorporating nitrogen into glass by melting phosphate in ammonia at high temperatures.[3] As a result, nitrogen is distributed uniformly throughout Gljach's glass when formed

[1] *See* Non-Final Office Action, mailed April 14, 2010, page 5.

[2] *See* Final Office Action, page 4.

[3] *See* Glajch, col. 5, lines 39-53 (citing Reidmeyer et al., J. Non-Crystalline Solids 1986, 85: 186-203, hereinafter "Reidmeyer").

from the melted liquid. Glajch states that nitriding the starting glass "is expected to decrease the dissolution rate of the solid in water and increase the chemical stability of the solid."[4]

Glajch's nitriding method is based on Reidmeyer's nitriding method. Reidmeyer teaches that the dissolution rate of glass treated with 11.75 % nitrogen (i.e., Reidmeyer/Glajch nitriding method) is 1000 times slower than the dissolution rate of base glass (i.e., glass not treated with nitrogen).[5] Yashchishin and Brow suggest that the dissolution rate of their treated glass is only about 3 to 6 times[6] and 10 times,[7] respectively, slower than the dissolution rate of base glass. As such, one of skill in the art would understand that glass treated using Yashchishin's or Brow's method would dissolve ***significantly faster*** (e.g., two orders of magnitude faster) than glass hypothetically made using Glajch's method. Even assuming Applicant accepts the USPTO's contention that Brow teaches a dissolution rate that is "up to 20 times better than base glass,"[8] this teaching is still far below the dissolution rate of Reidmeyer/Glajach.

In view of the foregoing, Applicant respectfully submits that the substitution of Brow's and/or Yashchishin's nitriding method for Glajch's/Reidmeyer's nitriding method is not "the simple substitution of one known, equivalent element for another." Indeed, as discussed above, this substitution would result in a significantly faster dissolution of the glass, i.e., result a less effective method. Accordingly, because the USPTO's proposed modification is not the substitution of known equivalents, there is no reason why one of skill in the art would have substituted Glajch's nitriding method, which seeks to decrease the dissolution rate, with a nitriding method that results in a faster dissolution rate than that of Glajch.

2. Brow's and Yashchisin's nitriding methods are specific for bulk glasses, whereas Reidmeyer's nitriding methods are undesirable for bulk glasses.

Brow teaches that bulk phosphorus oxynitride glasses prepared by melting oxide glass in dry ammonia atmospheres (i.e., Reidmeyer's method) results in the "tightening of the glass structure"

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[4] Glajach, col. 5, lines 45-47.

[5] *See* Reidmeyer, page 187, Table 1 (showing the dissolution rate of base glass as 1.1×10^{-3} compared to glass treated with 11.75 % nitrogen as 1.9×10^{-6}).

[6] *See* Yashchishin, page 8 (teaching that its method improves the chemical stability of phosphate glasses by 3 to 6 times).

[7] *See* Brow, abstract ("For example, the dissolution rate a sodium-barium phosphate glass (T_g = 345°C) decreased by over an order of magnitude"). One of skill in the art would understand that an order of magnitude means 10 times.

[8] *See* Final Office Action, page 8.

and "a significant reduction in bulk properties."[9] To avoid this problem, Brow suggests nitriding the surface by exposing the glass to dry ammonia at temperatures near the T_g temperature.[10] Brow teaches that this method improves durability "without greatly affecting desirable bulk glass properties."[11]

Yashchisin teaches that that glasses made using Reidmeyer's method result in glasses that are "impregnated with nitrogen in bulk" and thus "the properties typical of an oxide glass are changed."[12] Yashchisin suggests a method to avoid this undesirable glass, stating "To avoid such developments inadmissible for an optical glass, only the glass surface should be doped with nitrogen…"[13] To accomplish this, Yashchisin's nitriding method dopes glass below the T_g temperature.[14]

In view of the foregoing, one of skill in the art would understand that Glajch's/Reidmeyer's nitriding method and Brow's and/or Yashchisin's nitriding methods produce glasses having different properties. Indeed, Brow and Yashchisin teach methods for bulk glasses and characterize glasses made using Glajch's/Reidmeyer's nitriding methods as having undesirable properties for bulk glasses. Accordingly, one of skill in the art would understand that the substitution of Brow's and/or Yashchishin's nitriding methods for Glajch/Reidmeyer's nitriding method is not "the simple substitution of one known, equivalent element for another," but rather these are different methods for making different types of glasses.

B. There is no reason to substitute Glajch's nitriding method with a nitriding method that has a faster dissolution rate in the context of the claimed invention—implant materials for radiotherapy.

The claimed implant materials comprise a nitrogen-rich surface layer that assists in, for example, preventing the premature start of bioresorption and the premature release of radioisotopes. Delaying bioresorption and leakage of radioisotopes is advantageous for various radiotherapies such as the treatment of cancer.[15] Indeed, the claimed implant materials permit localized delivery of

[9] *See* Brow, page 172, second column, first full paragraph.

[10] *See id.* at page 172, second column, second full paragraph.

[11] *See id.*

[12] *See* Yashchishin, page 6, second column, second full paragraph.

[13] *Id.*

[14] *Id.* at Abstract.

[15] For example, claim 13 requires that the radioisotopes are present in an amount effective for radiation therapy of a tumor.

radioisotopes at a desired site (e.g., prostate). As such, one of skill in the art would appreciate that for the claimed implants to work for their intended purpose (i.e., radiotherapy), they must, *inter alia*, (i) maintain their integrity for a length of time sufficient to provide adequate therapy at a desired site; and (ii) prevent the premature release of the radioisotopes—i.e., the implants must not dissolve too quickly.

As discussed above, the proposed substitution of Brow's and/or Yashchishin's nitriding method for Glajch's/Reidmeyer's nitriding method would result in a glass that dissolves significantly faster than Glajch's/Reidmeyer's glass. Applicant submits that one of skill in the art would have no reason to make this substitution to arrive at an implant material that dissolves more quickly in the body. Rather, one of skill in the art would be discouraged from making such implant materials since they possess properties that are contrary to the intended purpose of the claimed implant materials. Accordingly, because the substitution of Brow's and/or Yashchishin's nitriding methods for Glajch's/Reidmeyer's nitriding methods would result in less effective implant materials for radiotherapy, one of skill in the art would have no reason to make this substitution.

In view of the foregoing, Applicant submits that there is no reason to combine Brow and/or Yashchishin with Glajch. Accordingly, Applicant respectfully requests withdrawal of this rejection.

C. Combining Brow's and/or Yashchishin's nitriding methods with Glajch would not produce the claimed implant materials.

As discussed above, the claimed implant materials for radiotherapy comprise a nitrogen-rich surface layer. As such, one of skill in the art would understand that, in order for the claimed implant materials to work for their intended purpose, the nitrogen-rich surface layer would necessarily surround the implant materials.

Glajch teaches a method of making phosphate glass particles by melting phosphate glass into a "bulk" glass and crushing the phosphate glass into particles.[16] Brow and Yashchishin disclose methods of nitriding "bulk" materials.[17]

Assuming one of skill in the art had a reason to apply Brow's and/or Yashchishin's methods to Glajch, which they would not, the skilled artisan would nitride Glajch's bulk glass and then crush the nitrided bulk glass into particles. One of skill in the art would understand that crushing bulk glass into particles will necessarily result in particles that do not have any nitrogen, let alone a

[16] *See* Glajch, col. 12, lines 7-17, Example 2.

[17] *See* Brow, page 172, under "Introduction" (disclosing glasses designed for sealing to high expansion metals); *see also* Yashchishin, page 8, last paragraph (disclosing optical glasses for lenses).

nitrogen-rich surface layer (e.g., a particle formed from the middle of the bulk glass would not have any nitrogen on its surface). Indeed, these particles would not result in the claimed implant materials, nor would they be useful for radiotherapy.[18] Accordingly, even assuming one of skill in the art substituted Brow's and/or Yashchishin's nitriding methods for Glajch's nitriding method, this hypothetical method would not produce the claimed implant materials.

In response to this argument, the USPTO asserts (i) Brow and Yashchishin "were not used to teach nitriding bulk glasses and then crushing the nitrided bulk glass into particles but were used to teach of nitriding phosphate glasses wherein the method … can be applied to particles of smaller sizes"; and (ii) "nothing in the references exclude nitriding particles …".[19]

Applicant respectfully points out, however, that Brow and Yashchishin specifically teach nitriding bulk glasses—not small particles. In paricular, Brow teaches nitriding to finished glass seals in order to preserve bulk properties such as thermal expansion, and Yashchinsin teaches nitriding the surface of a finished lens.[20] These teachings cannot be ignored. Indeed, a "prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention."[21]

The USPTO appears, however, to ignore Brow's and Yashchishin's actual teachings (i.e., nitriding bulk glasses), and nonetheless asserts that they can be applied to small particles simply because "nothing in the references exclude nitriding particles." This statement is not sufficient to establish a *prima facie* case of obviousness. Indeed, "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness."[22] Accordingly, because the USPTO has not provided a reason why one of skill in the art would ignore Brow's and Yashchishin's actual teachings, and attempt to apply certain aspects of these teachings to a completely different material, Applicant respectfully submits that the USPTO has not established a *prima facie* case of obviousness.

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[18] These particles would also render Glajch unsuitable for its intended purpose. *See* Section D.

[19] Final Office Action, page 10.

[20] *See* Brow, page 172; *see also* Yashchishin, page 6. If Brow's glass seal is broken into small particles they will not function as a seal. Similarly, if Yashchisin's lens is crushed into small particles they will not function as a lens.

[21] M.P.E.P. § 2141.02, VI.

[22] *See* M.P.E.P. § 2141 (citing *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006); *see also KSR*, 127 S. Ct. at 1741 (quoting Federal Circuit statement with approval).

Applicant also notes that because (i) Glajch teaches making particles by crushing bulk glasses; and (ii) Brow and Yashchishin teach nitriding bulk glasses, it logically follows that if these methods were combined, as the USPTO contends, one of skill in the art would nitride Glajch's bulk glass using Brow's and/or Yashchishin's method and then crush the bulk glass to make particles. Therefore, as discussed above, assuming that one of skill in the combined Glajch with Brow and/or Yashchishin, as suggested by the USPTO, they would not have arrived at the claimed implant materials.

D. The proposed modification would render Glajch unsatisfactory for its intended purpose and change the principle of Glajch's operation.

As discussed above, Glajch suggests incorporating nitrogen into glass by melting phosphate in ammonia at high temperatures, thereby distributing nitrogen uniformly throughout the glass. Glajch states that nitriding the starting glass "is expected to decrease the dissolution rate of the solid in water and increase the chemical stability of the solid."[23] Glajch also teaches making phosphate glass particles by melting phosphate glass into a "bulk" glass and crushing the phosphate glass into particles.[24] These particles are purportedly then used in therapeutic methods.[25]

The USPTO appears to suggest that one of skill in the art would combine and modify the references by (i) substituting Glajch's nitriding method (i.e., nitriding uniformly throughout a particle) with Brow's and Yashchishin's nitriding method (i.e., nitriding to provide a nitrogen surface layer); and (ii) modifying Brow's and/or Yashchishin's nitriding method (i.e., nitriding bulk glass) by nitriding Glajch's particles after they have been crushed.

Applicant respectfully submits that the proposed modifications would render Glajch's methods unsatisfactory for its intended purpose and would change the principle of Glajch's operation.[26] First, Glajch sought to decrease the dissolution rate of the solid in water and increase the chemical stability of the solid by incorporating nitrogen uniformly throughout his glass. By applying Brow's and Yashchishin's nitriding method, as discussed above, the glass would dissolve

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[23] Glajch, col. 5, lines 45-47.

[24] *See id.* col. 12, lines 7-17, Example 2.

[25] *See id.* at col. 1 ("Field of Invention").

[26] *See* M.P.E.P. 2143.01, V ("If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)"); VI ("If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)").

significantly faster than Glajch's glass and have different properties. Second, Glajch suggests a specific method of nitriding (i.e., incorporating nitrogen by melting phosphate in ammonia at high temperatures) and making glass particles (i.e., by crushing bulk glasses) for the purported use of radiotherapy. The USPTO's proposed modification eliminates one step of Glajch's process (e.g., incorporating nitrogen uniformly throughout the glass) and adds another step of nitriding the particle surface after crushing. These changes would inevitably result in a different, less effective composition than taught by Glajch. Accordingly, because the proposed modifications would render Glajch's methods unsatisfactory for its intended purpose and would change the principle of Glajch's operation, Applicant respectfully submits that the proposed combination of Glajch with Brow and/or Yashchishin do not render any of the claims obvious.

E. The combination of references does not teach or suggest various dependent claims.

1. Claim 5

Claim 5 is directed to resorbable implant materials comprising a phosphate based glass matrix comprising a calcium to phosphate ratio from about 0.33 to about 1.67.

The combination of references does not teach or suggest such implant materials. Indeed, the only asserted Ca:P ratios disclosed in any of the references is taught by Glajch.[27] Glajch teaches that the Ca:P molar ratios of particles made by mixing $Ca(PO_3)_2$ and $NaPO_3$ are 0.25, 0.167, 0.083, 0.045[28]—i.e., less than the claimed ratio of 0.33-1.67. Accordingly, because the combination of references does not teach or suggest each and every claim element, the combination does not render claim 5 obvious.

2. Claim 8

Claim 8 is directed to resorbable implant materials comprising a phosphate based matrix, wherein at least a part of the phosphate based matrix contains a borate or silicate.

The combination of references does not teach or suggest such implant materials. Indeed, nowhere in the Final Office Action or in the Non-Final Office Action, mailed April 14, 2010, is it asserted that the references teach or suggest a phosphate based matrix containing borate or silicate. Accordingly, because the combination of references does not teach or suggest every claim element,

[27] *See* Non-Final Office Action, mailed April 14, 2010, page 5.

[28] *See id.* (teaching particles comprising $Ca(PO_3)_2$ and $NaPO_3$ in a molar ratio of Ca:Na of 1:2, 1:4, 1:10, and 1:20). For example, it will be understood that a Ca:Na ratio of 1:2 means that there will be one molecule of $Ca(PO_3)_2$ for every two molecules of $NaPO_3$, i.e., one calcium molecule for every four phosphate molecules, resulting in a Ca:P ratio of 1:4 or 0.25.

the combination does not render claim 8 obvious.

In view of the foregoing, Applicant respectfully requests withdrawal of this rejection.

Claims 1-5, 8-11, 13-16, 18-20, 36, and 37 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Glajch in view of Brow and Yashchisin, and in further view of Gilchrist et al. (U.S. Patent No. 6,143,318, hereinafter "Gilchrist").

As discussed above, the combination of Glajch, Brow, and Yashchishin does not teach or suggest resorbable implant materials comprising, *inter alia*, a nitrogen-rich surface layer formed on the resorbable base glass matrix, the surface layer being of greater durability than the base glass matrix. Gilchrist does not remedy the deficiencies of Glajch, Brow, and Yashchishin. Indeed, Gilchrist is silent regarding the use of nitrogen, let alone forming a nitrogen-rich layer on the surface of a resorbable base glass matrix. Accordingly, because the combination of Glajch, Brow, Yashchishin, and Gilchrist does not teach or suggest each and every element of claim 1 or 36, this combination does not render obvious any of the claims.

In view of the foregoing, Applicant respectfully requests withdrawal of this rejection.

Claims 1-8, 10-20, 36, and 37 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Glajch in view of Brow and Yashchisin, and in further view of Wong et al. (U.S. Pub. No. 2004/0131543, hereinafter "Wong").

As discussed above, Glajch, Brow, and Yashchishin does not teach or suggest resorbable implant materials comprising, *inter alia*, a nitrogen-rich surface layer formed on the resorbable base glass matrix, the surface layer being of greater durability than the base glass matrix. Wong does not remedy the deficiencies of Glajch, Brow, and Yashchishin. Indeed, Wong is silent regarding the use of nitrogen, let alone forming a nitrogen-rich layer on the surface of a resorbable base glass matrix. Accordingly, because the combination of Glajch, Brow, Yashchishin, and Wong does not teach or suggest each and every element of claim 1 or 36, this combination does not render obvious any of the claims.

In view of the foregoing, Applicant respectfully requests withdrawal of this rejection.

CONCLUSION

In view of the above remarks, early notification of a favorable consideration is respectfully requested. An indication of allowance of all claims is respectfully requested.

This response is being filed within the three-month time period set forth in the Final Office Action. Accordingly, no fees are due. Should any fees be due to enter and consider this response, however, the USPTO is authorized to charge these fees to **Deposit Account No. 50-0206**.

If the Examiner has any questions relating to this response, or the application in general, she is respectfully requested to contact the undersigned so that prosecution of this application may be expedited.

Respectfully submitted,

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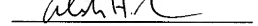

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